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CASE REPORT | SMALL BOWEL

Posttransplant Lymphoproliferative Disorder of the Small Bowel as an Unexpected Cause of Iron Deficiency Anemia Decades after Heart Transplantation

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ABSTRACT

Although rare, gastrointestinal posttransplant lymphoproliferative disorder (PTLD) can lead to abdominal pain or gastrointestinal bleeding in patients with a history of solid-organ transplantation. We describe a case of isolated gastrointestinal PTLD in a patient who presented with acute on chronic iron deficiency anemia 26 years after heart transplant. A comprehensive endoscopic evaluation with video capsule endoscopy and small bowel enteroscopy revealed a large cratered ulceration in the small bowel with abnormal mucosal changes, which led to the diagnosis of PTLD.

INTRODUCTION

Iron deficiency anemia and gastrointestinal (GI) bleeding are frequently seen among patients with multiple cardiac comorbidities, including valvular heart disease, cardiomyopathies, and cardiogenic shock. While common etiologies of bleeding include angioectasias, ulcers, and ischemic injury, neoplastic processes, including posttransplant lymphoproliferative disorder (PTLD), are an important consideration in patients who have undergone solid organ transplantation. PTLD is the most common malignancy among transplant patients, comprising 25% of all posttransplant malignancies. GI-isolated PTLD is an uncommon presentation and may present with abdominal pain or bleeding.

CASE REPORT

A 65-year-old man with a history of orthotopic heart transplant 26 years prior and chronic immunosuppression with cyclosporine, azathioprine, and prednisone presented to the hospital with dyspnea on exertion. His additional comorbidities included severe aortic stenosis and heart failure of the transplanted heart, as well as paroxysmal atrial fibrillation (on warfarin) and chronic kidney disease. He was found to be anemic with hemoglobin 7.5 g/dL, compared to 11.0 g/dL 6 months prior, so the inpatient gastroenterology team was consulted. Colonoscopy revealed internal hemorrhoids, non-bleeding colonic diverticuli, and several small polyps, which were removed. Upper endoscopy revealed a superficial clean-based gastric ulcer in the body and a few small antral erosions, which were felt to be the source of his anemia. Biopsies of the stomach revealed only reactive gastropathy and chronic inflammation. He was started on a proton-pump inhibitor twice daily and discharged home.

Two weeks following discharge, he presented again, this time with mixed cardiogenic and septic shock due to pneumonia, which resolved with broad-spectrum antibiotics. His labs were notable for hemoglobin as low as 6.0 g/dL, iron 34 μg/dL, and ferritin 21 ng/mL, consistent with iron-deficiency anemia. At this time, the patient reported solid

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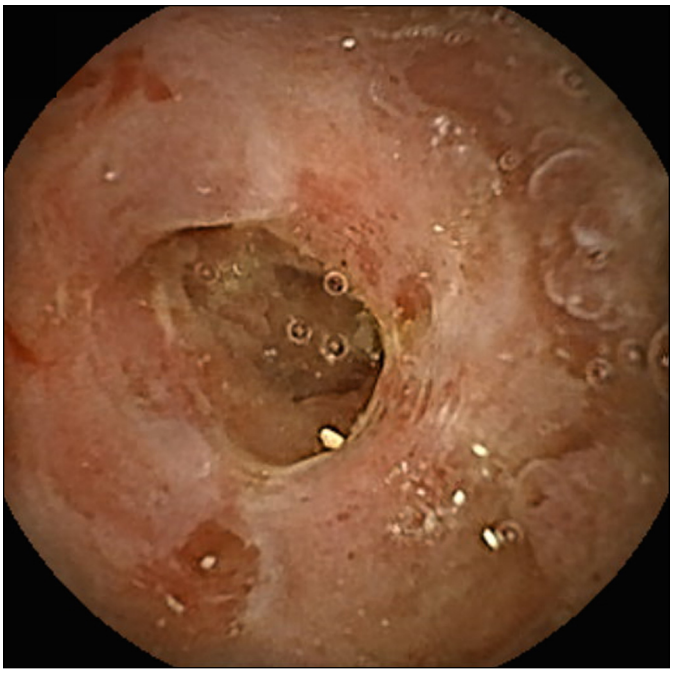

Figure 1. Video capsule endoscopy demonstrating multiple areas of ulceration within the small bowel.

black stools, which were his baseline since starting oral iron supplementation a year prior. Given his worsening anemia, computed tomography with GI bleeding protocol was considered, but this was deferred given the patient's advanced renal disease. He underwent video capsule endoscopy, which revealed areas of ulceration with heaped up mucosa and active bleeding in the small bowel (Figure 1). These ulcers were thought to be due to ischemic injury in the setting of recent septic shock and the patient's known severe atherosclerotic vascular disease. His anemia persisted despite repeated transfusions. Magnetic resonance enteroscopy did not reveal any obvious intraluminal masses or lesions. Subsequently, a small bowel enteroscopy with a pediatric colonoscope revealed a large cratered ulcer with an adherent clot in the distal duodenum, surrounded by edematous and irregular mucosa (Figure 2). Biopsies of the ulcer edge revealed monomorphic posttransplant lymphoproliferative disorder (PTLD), plasmacytoma-like (Figure 3). Serum Epstein-Barr virus (EBV) polymerase chain reaction remained undetectable. Staging positron emission tomography–computed tomography demonstrated enhancement only in the the small intestine, and there was no evidence of PTLD on bone marrow biopsy. The patient's chronic immunosuppression regimen was decreased, and he was initiated on rituximab prior to hospital discharge.

DISCUSSION

The rates of PTLD vary by transplant type; 1–6% in heart transplants, 1–3% in kidney or liver transplants, 4–10% in lung

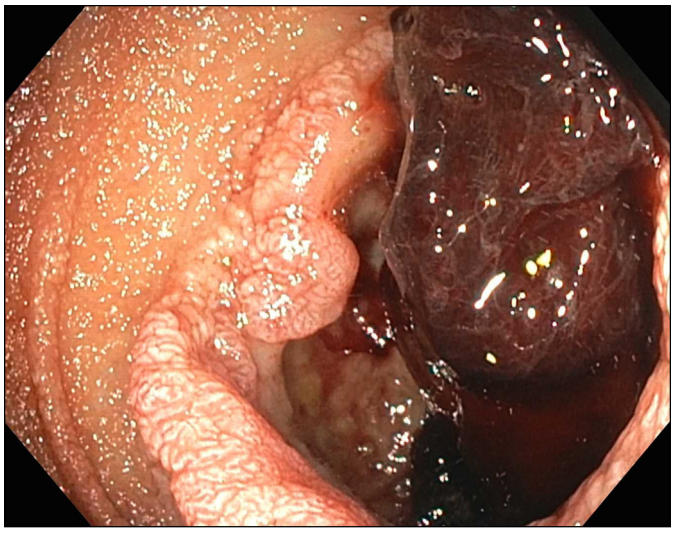

Figure 2. Small bowel enteroscopy showing a deep, cratered ulcer with an adherent clot in the distal duodenum.

transplants, and in up to 20% in small intestine transplants.[1] The average time between transplant and diagnosis is approximately 5.5 years, although early cases can develop during the first year after transplant. Most commonly, patients present with fever and lymphadenopathy; however, extranodal involvement will be present in two-thirds of cases. As the majority of these disorders are associated with EBV, EBV seroconversion is an important risk factor for developing PTLD. EBV-negative recipients who are transplanted an organ from an EBV-positive donor are at a particularly high risk for PTLD.[2] Male gender, white race, and younger age at transplantation are additional independent risk factors for developing PTLD.[1,3] Lastly, there is a known correlation between type and duration of immunosuppression and the risk of developing PTLD. Therefore, reduction in immunosuppression is the first step in treating PTLD; 25–63% of adults will respond to reduction in immunosuppression alone.[4] Chemotherapy, anti-B-cell antibodies, or cytokine-based therapies may be used in addition to reduction of immunosuppression for systemic treatment of PTLD.

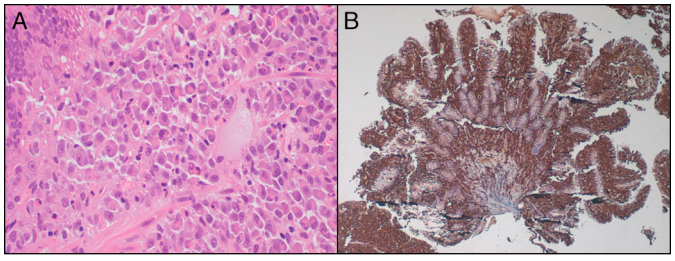

Figure 3. (A) High-power field of small bowel biopsies demonstrating numerous atypical plasma cells with irregular nuclear contours and prominent nucleoli. (B) Diffuse staining for κ light chain in the plasma cells of the lamina propria, consistent with a clonal process.

Studies demonstrate that up to half of patients with PTLD have evidence of disease in the small bowel, colon, or mesenteric lymph nodes.[5,6] However, isolated PTLD of the GI tract is rare. As PTLD is more common among pediatric patients, isolated GI PTLD is best described in pediatric literature. O'Connor et al. described 6 cases diagnosed in children after liver transplant who were suspected to have PTLD given symptoms such as anemia, failure to thrive, vomiting, or abdominal pain. The colon and stomach were the most common sites involved, with rubbery, raised, and ulcerated lesions seen on endoscopy.[7] Additional pediatric case reports describe GI bleeding as the presenting symptom leading to endoscopic diagnosis of PTLD with ulcerations in the small intestine.[8,9] Among adults, the only case series of isolated GI PTLD described 12 cases in lung-transplant patients. Of these, 7 cases involved the colon and 5 cases involved the small bowel. Presenting symptoms included abdominal pain, constipation, and hematochezia. The median time to presentation after transplant was 2.9 years, and most demonstrated ulceration and/or perforation on endoscopy.[10] There are very few additional reports of isolated PTLD of the GI tract in the adult transplant population.[6,11]

Our case represents a rare endoscopic diagnosis of isolated PTLD of the small intestine in a patient presenting with iron-deficiency anemia without overt GI bleeding or abdominal pain. This case is particularly unique as it represents a diagnosis of PTLD more than 25 years after solid-organ transplantation. Though less common than other causes of iron-deficiency anemia in patients with valvular heart disease or cardiomyopathies, such as Heydes syndrome, angioectasias, and ischemia, PTLD must be considered in posttransplant patients presenting with GI bleeding, ulcers, or perforation.

DISCLOSURES

Author contributions: All authors interpreted the data, and wrote and revised the manuscript. A. Siegel is the article guarantor.

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Informed consent was obtained for this case report.

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REFERENCES

1. LaCasce AS. Post-transplant lymphoproliferative disorders. *Oncologist*. 2006;11(6):674–80.
2. Al-Mansour Z, Nelson BP, Evens AM. Post-transplant lymphoproliferative disease (PTLD): Risk factors, diagnosis, and current treatment strategies. *Curr Hematol Malig Rep*. 2013;8(3):173–83.
3. Wasson S, Zafar MN, Best J, Reddy HK. Post-transplantation lymphoproliferative disorder in heart and kidney transplant patients: A single-center experience. *J Cardiovasc Pharmacol Ther*. 2006;11(1):77–84.
4. Taylor AL, Marcus R, Bradley JA. Post-transplant lymphoproliferative disorders (PTLD) after solid organ transplantation. *Crit Rev Oncol Hematol*. 2005;56(1):155–67.
5. Hachem RR, Chakinala MM, Yusen RD, Lynch JP, Aloush AA, Patterson GA, Trulock EP. Abdominal-pelvic lymphoproliferative disease after lung transplantation: Presentation and outcome. *Transplantation*. 2004;77(3):431–7.
6. Haverkos BM, Oza VM, Johnson A, Walker J, Shana'ah A. Rare presentation of post-transplant lymphoproliferative disorder isolated to gastroesophageal junction. *World J Gastrointest Oncol*. 2013;5(12):230.
7. O'Connor JA, Cogley C, Burton M, Lancaster-Weiss K, Cordle RA. Posttransplantation lymphoproliferative disorder: Endoscopic findings. *J Pediatr Gastroenterol Nutr*. 2000;31(4):458–61.
8. Ho EY, George V, McCracken M, Ostroff JW. A 13-year-old boy with post-transplantation lymphoproliferative disorder presenting with obscure gastrointestinal bleeding: A case report. *F1000Research*. 2014;3:88.
9. Sebire NJ, Malone M, Risdon RA, Ramsay AD. Epstein-Barr virus: Associated lymphoproliferative disorder presenting as apparently isolated gastrointestinal lesions in childhood. *Pediatr Dev Pathol*. 2005;8(1):88–91.
10. Shitrit D, Shitrit AB, Dickman R, Sahar G, Saute M, Kramer MR. Gastrointestinal involvement of posttransplant lymphoproliferative disorder in lung transplant recipients: Report of a case. *Dis Colon Rectum*. 2005;48(11):2144–7.
11. Grivas PD. Post-transplantation lymphoproliferative disorder (PTLD) twenty years after heart transplantation: A case report and review of the literature. *Med Oncol*. 2011;28(3):829–34.